

REMARKS/ARGUMENTS

Reexamination and reconsideration of this Application, withdrawal of the rejection, and formal notification of the allowability of all claims as now presented are earnestly solicited in light of the above amendments and remarks that follow.

Claims 2-3, 12-21, and 35-38 stand rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of U.S. Patent No. 5,484,601 to O'Leary et al., U.S. Patent No. 5,385,887 to Yim et al., and U.S. Patent No. 6,030,635 to Gertzman et al. The Examiner relies upon the O'Leary reference as teaching a flowable demineralized bone matrix composition comprising an organic carrier and a thickener, such as a cellulosic ester. The Examiner admits that O'Leary is silent with respect to the use of calcium sulfate or bone allograft, but notes that O'Leary states that "a variety of substances" can be introduced into the bone particles, including "inorganic elements." The Examiner relies upon the Yim reference as teaching a composition for delivering osteogenic proteins that includes calcium sulfate. The Examiner alleges that it would be obvious to include the calcium sulfate of Yim in the composition of O'Leary because Yim teaches that calcium sulfate improves handling, moldability, and consistency, and reduces set-up time. The Examiner relies upon the Gertzman reference as teaching the use of allograft bone in a malleable putty for filling bone defects and concludes it would be obvious to include allograft bone in the composition of O'Leary. Applicants respectfully traverse this rejection.

Applicants respectfully submit that one of ordinary skill in the art would have no motivation to combine the three references of the rejection in the manner contemplated by the Examiner. Specifically, the art provides no motivation for combining the Yim and Gertzman references with the O'Leary reference in the manner relied upon by the Examiner.

The O'Leary reference is directed to a flowable composition comprising demineralized bone powder and an organic liquid carrier, and suggests that a thickener may be added to the composition to maintain the bone powder in suspension. The O'Leary reference teaches that the composition can be applied to the site of a bone defect in the form of, for example, a highly viscous paste. Thus, the O'Leary reference is directed to a composition designed to provide demineralized bone powder in a form suitable for surgical use.

The Examiner relies on language in the Yim reference regarding reduction in set-up time and improvement in handling, moldability and consistency as evidence of a motivation to combine the calcium sulfate hemihydrate of Yim with the formulation of O'Leary. However, Yim does not provide a general suggestion that calcium sulfate provides such advantages in all bone graft compositions. Instead, the Yim reference only suggests that a calcium sulfate hemihydrate-containing substance (CSHS) provides such advantages when combined with the formulation described in U.S. Pat. No. 5,171,579 (see column 2, lines 51-65). Yim only suggests a CSHS provides such advantages in the context of a formulation comprising osteogenic proteins, autogenous blood, and a porous particulate polymer matrix, such as a copolymer of lactic acid and glycolic acid (PLGA). There is no suggestion in the Yim reference that such improved properties would be expected in any other formulation. Yim merely teaches that, "[t]o reduce the preparation time and improve the above formulation's handling characteristics"(emphasis added), a CSHS can be added. The "above formulation" is the formulation described in the '579 patent, which includes an osteogenic protein, autogenous blood, and a porous particulate polymer matrix. Since the composition in the O'Leary reference is not a combination of osteogenic proteins with autogenous blood and a porous particulate polymer matrix such as PLGA, there would be no motivation to combine the CSHS of Yim with the composition described in O'Leary for the reasons suggested by the Examiner.

The O'Leary formulation comprises demineralized bone powder and an organic liquid, and such a composition is markedly dissimilar to the composition described in Yim as needing improvement in set-up time, moldability, etc. Further, there is nothing in the O'Leary reference to suggest a problem with moldability, consistency, etc. of the formulation described therein that might lead one of ordinary skill in the art to seek an additive to address such a problem. Indeed, the O'Leary patent seems to suggest that the consistency of the "flowable" material can be adjusted simply by altering the amount of the liquid component (column 3, lines 28-35).

In a further effort to bolster the proposed combination of Yim with O'Leary, the Examiner argues that the Yim and O'Leary formulations are "sufficiently similar" such that one of ordinary skill would be aware that calcium sulfate hemihydrate "would not impair or otherwise negatively affect" the O'Leary composition. However, the simple understanding by

one of ordinary skill in the art that the addition of a certain compound to a composition would not negatively affect that composition is insufficient to motivate one to make such a combination. The art must provide a positive motivation to make the combination suggested in the rejection rather than simply fail to teach against such a combination.

The Examiner also relies on a general recitation in O'Leary that "a variety of substances" can be added to the bone particles. However, such a broad and non-specific reference to optional ingredients, even one that mentions the addition of "inorganic elements", is clearly insufficient to provide the requisite motivation to include a specific inorganic compound such as calcium sulfate hemihydrate. Such a general teaching has no bearing at all on the specific question of whether one of ordinary skill in the art would have been motivated to combine the calcium sulfate hemihydrate teaching of Yim with the formulation in O'Leary.

Thus, as noted above, it is respectfully submitted that one of ordinary skill in the art would have no motivation to combine the teachings of Yim with the teachings of O'Leary as contemplated by the Examiner and Applicants respectfully request reconsideration and withdrawal of the rejection of record for this reason.

In addition, Applicants respectfully submit that there is no motivation to combine the teachings of the Gertzman reference with the teachings of O'Leary. The composition described in the Gertzman reference is so fundamentally distinct from the composition described in the O'Leary reference that one of ordinary skill in the art would view such differences as weighing against the combination suggested by the Examiner.

The Gertzman reference is directed to a malleable paste for filling bone defects, the composition including a high molecular weight hydrogel and an aqueous solution as the carrier for demineralized bone powder. The O'Leary reference is clearly not directed to compositions including a high molecular weight hydrogel component as a carrier ingredient for demineralized bone, and for this reason, one of ordinary skill in the art would not view the teachings of Gertzman as relevant to the O'Leary composition.

Further, the Gertzman reference specifically contrasts the teachings of the O'Leary reference. In the background section, the Gertzman reference points out numerous disadvantages associated with GRAFTON, a commercial embodiment of the composition of O'Leary. For instance, Gertzman notes that the glycerol carrier of GRAFTON has a very low molecular weight and low viscosity at higher temperature, which contribute to making the composition "runny" when used in surgery. The Gertzman reference notes that one method of overcoming this negative characteristic of GRAFTON is to use larger bone particles. However, the use of larger bone particles is less preferred for a variety of reasons mentioned in Gertzman. Additionally, Gertzman suggests "glycerol and other similar low molecular weight organic solvents are toxic and irritating" (column 3, lines 22-23). The Gertzman reference clearly indicates that the composition described therein is intended to overcome the deficiencies of GRAFTON and similar compositions, such as the compositions described in O'Leary. Gertzman et al. expressly note that their composition "avoids the toxic problems ... of the low molecular weight organic solvents of the prior art" (column 4, lines 15-17).

Thus, it is clear that Gertzman goes to great lengths to distance the compositions described therein from the teachings of O'Leary, which utilize a low molecular weight organic carrier component. In light of this clear teaching away from O'Leary, there would be no motivation to combine the teachings of Gertzman with the O'Leary reference in the manner contemplated by the Examiner. For this additional reason, Applicants request reconsideration and withdrawal of the rejection.

It is believed that all pending claims are now in condition for immediate allowance. It is requested that the Examiner telephone the undersigned should the Examiner have any comments or suggestions in order to expedite examination of this case.

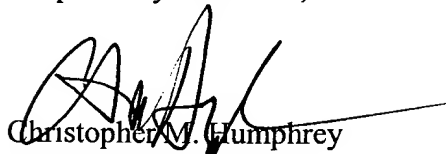
It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

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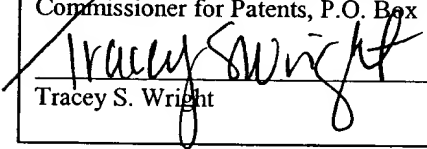
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